Seminar Notice

Involvement of non-selective channels in several skeletal muscles pathologies

by

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Abstract

In mammals, the sarcolemma of skeletal myofibers is rather impermeable to Ca\(^{2+}\), and monovalent ions can diffuse across it through ion selective channels, relevant for action potentials that elicit a single twitch. However, repetitive twitches activate a non-selective channel constituted of pannexin1 protein (Panx1 channel), which allow ATP release needed for potentiation of contraction. Moreover, myofibers under diverse pathological conditions [e.g., denervation, chronic glucocorticoid treatment, sepsis and mutations of specific proteins (e.g., dystrophin and dysferlin)] show de novo expression of several non-selective membrane channels [e.g., connexin hemichannels, P2X\(_7\) receptor and TRPV2 channel], which are not detected in myofibers of mice models of cancer or disuse. The non-selective channels expressed in pathological conditions are permeable to Ca\(^{2+}\) and thus, contribute to increase the intracellular free Ca\(^{2+}\) concentration that activates protein degradation pathways known to lead to atrophy. Studies on the relative importance of each non-selective channel in different diseases are underway, and so far we known that muscles of Panx1 or P2X\(_7\) receptor KO mice are not protected upon denervation-induced changes. In contrast, myofibers deficient in connexin43 and connexin45 show a strong protection in all aforementioned pathological conditions. In addition, mice treated with a selective and potent Cx hemichannel blocker do not manifest muscular atrophy. Hence, we propose these non-selective channels as good molecular targets to prevent muscle degeneration in several pathological conditions.

Date : 21 November 2017 (Tuesday)
Time : 4:00 pm
Venue : Room 2405 (near Lift 17/18)
HKUST

(Host faculty : Dr. Tom CHEUNG)

All are Welcome!